Finding the Needle…Again…and Again…and Again:
Lessons Learned from NCI Programs

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Health Sciences Director

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Office of the Director, National Cancer Institute (NCI)
National Institutes of Health (NIH)

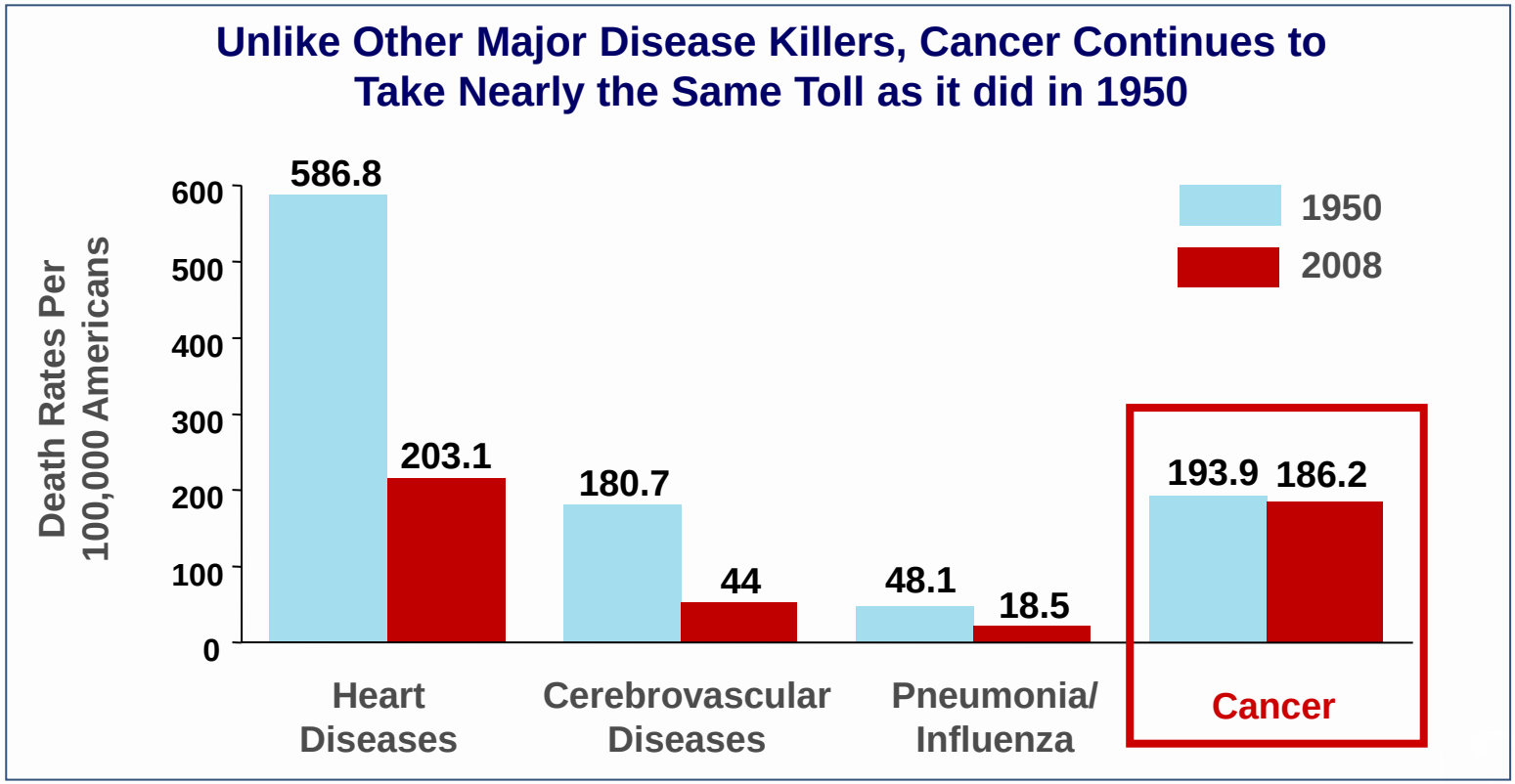
World CTC Summit, Boston MA

November 13, 2012

NCI Alliance for Nanotechnology in Cancer | Office of Physical Sciences Oncology | Office of Cancer Clinical Proteomics Research | Office of Cancer Genomics | The Cancer Genome Atlas

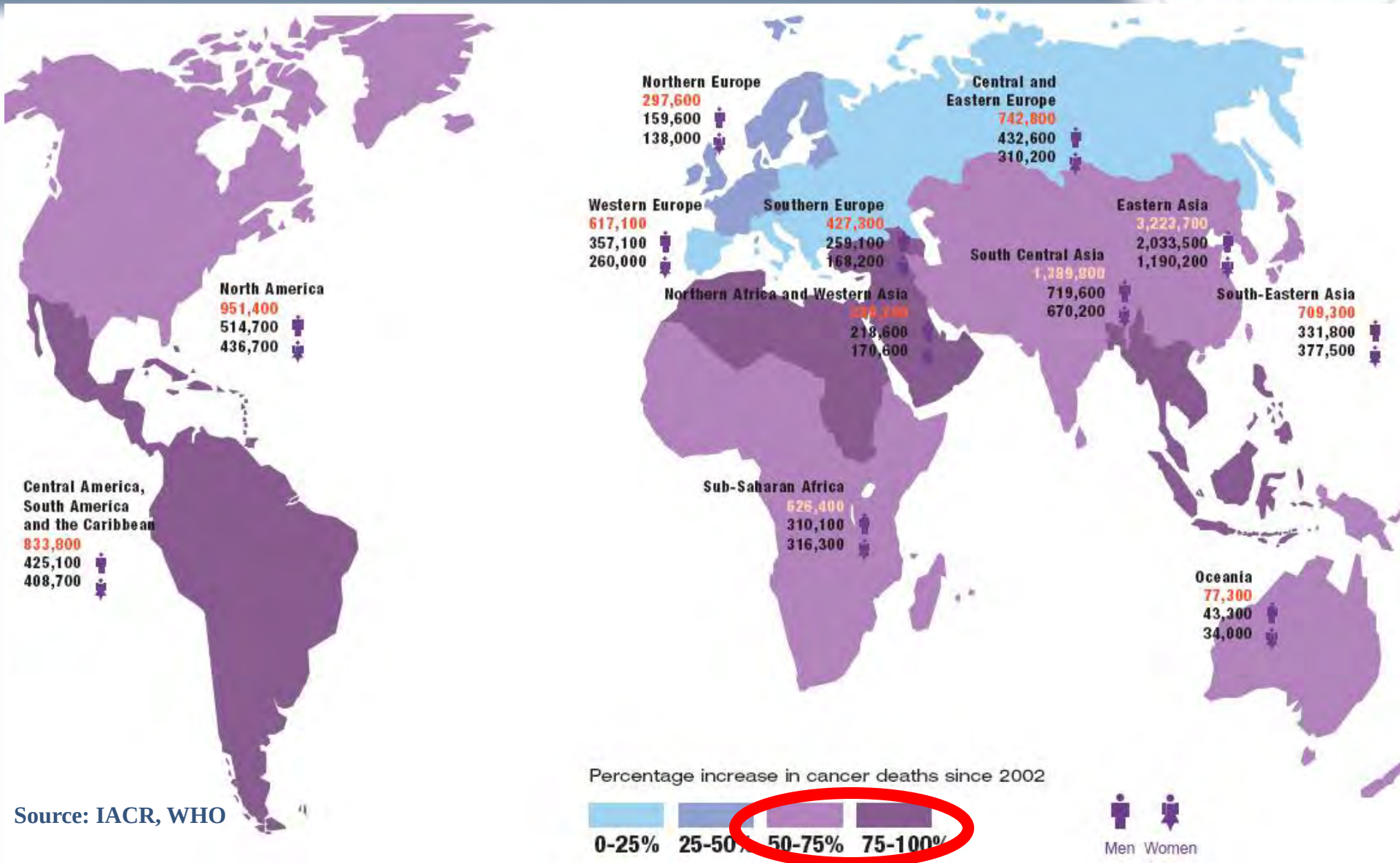
In the U.S., Cancer Continues to Represent an Enormous Burden

- **569,490** Americans died of cancer in 2010
- **1,529,560** Americans will be diagnosed with cancer this year
- **$124.6 billion** in 2010 for cancer healthcare costs



Source for 2010 deaths and diagnoses: American Cancer Society (ACS) 2010 Cancer Facts & Figures; Atlanta, Georgia
Source for 2008 age-adjusted death rate: National Center for Health Statistics, NCHS Public-use file for 2008 deaths.

Global Burden: By 2020, Cancer Mortality 10 M/yr (Incidence 16 M/yr)



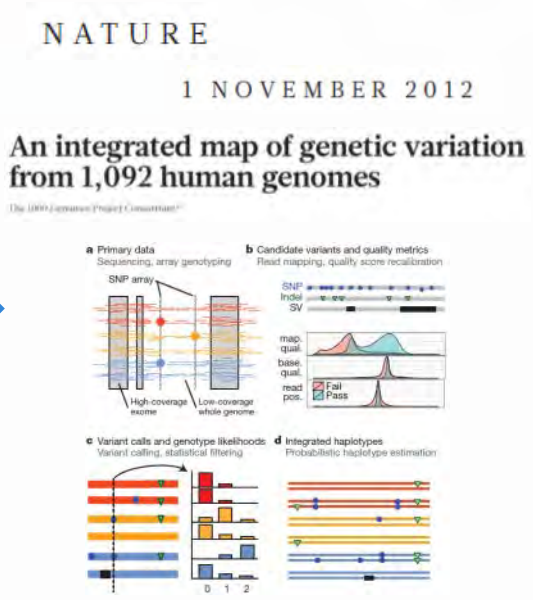
Source: IACR, WHO

Unprecedented Amount of Scientific Knowledge: Omics(ssss)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

2001

2010



2012

1923 — 2005 — 2012

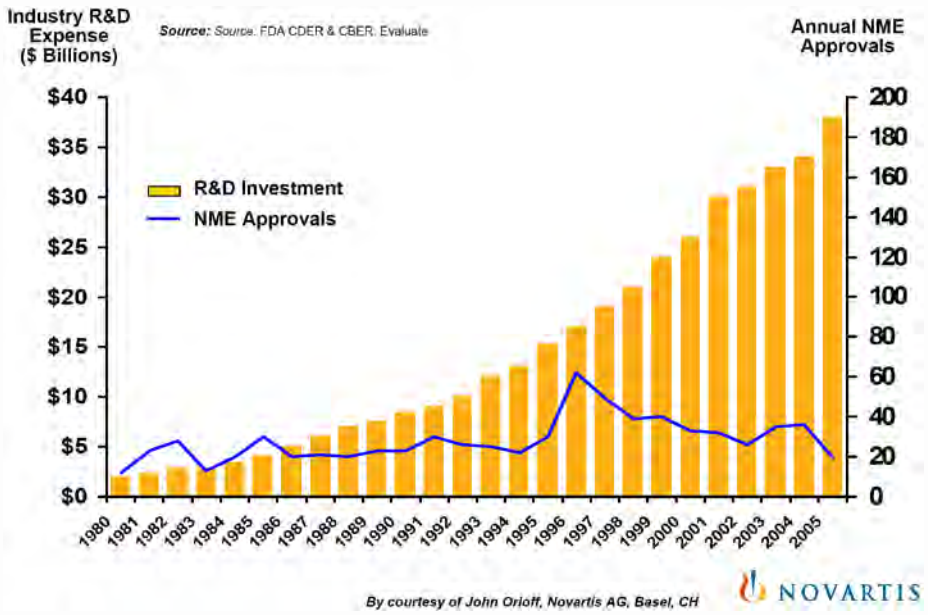
49,024 pubs | 54,587 pubs | **87,793** pubs | **38,506** pubs

ISI search for genomics, proteomics, transcriptomics, metabolomics, phenomics, interactomics, glycomics

Is More Knowledge Yielding More Solutions for Patients?

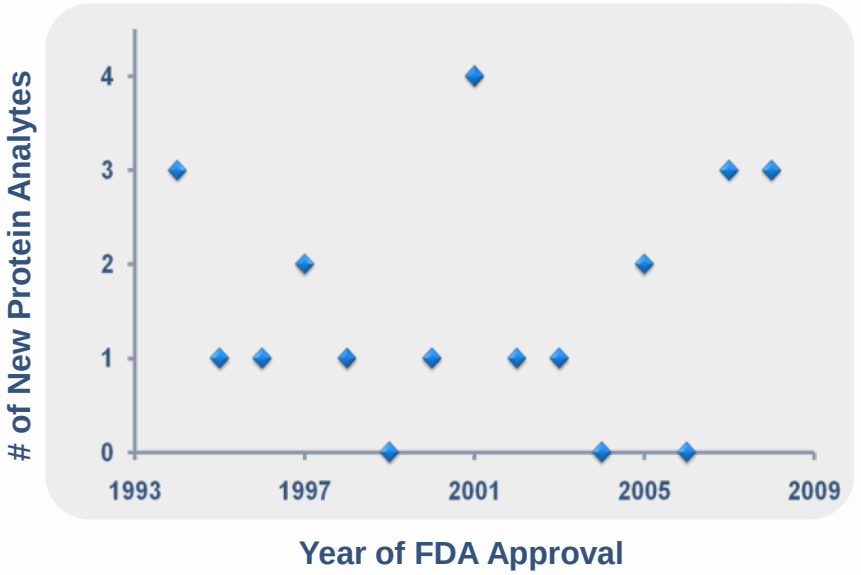
CENTER for STRATEGIC SCIENTIFIC INITIATIVES

Drug Discovery and Development



- 10 – 15 years at ~ $1.8 billion*
- 2007: 19 NMEs [lowest since 1983]
- 2008: 21 NMEs [**29%** new-in-class]
- 2009: 24 NMEs [**17%** new-in-class]

Diagnostic Biomarkers



- Averaging 1.5 FDA approvals per year†
- 1000's of samples
- Balancing complexity of biology against heterogeneity of patients

Maybe…but can it be more efficient?

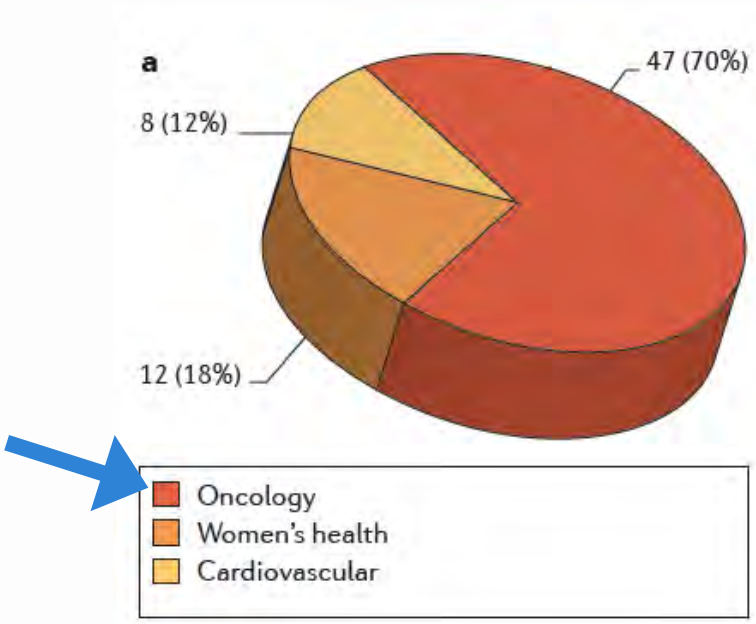
NATIONAL CANCER INSTITUTE

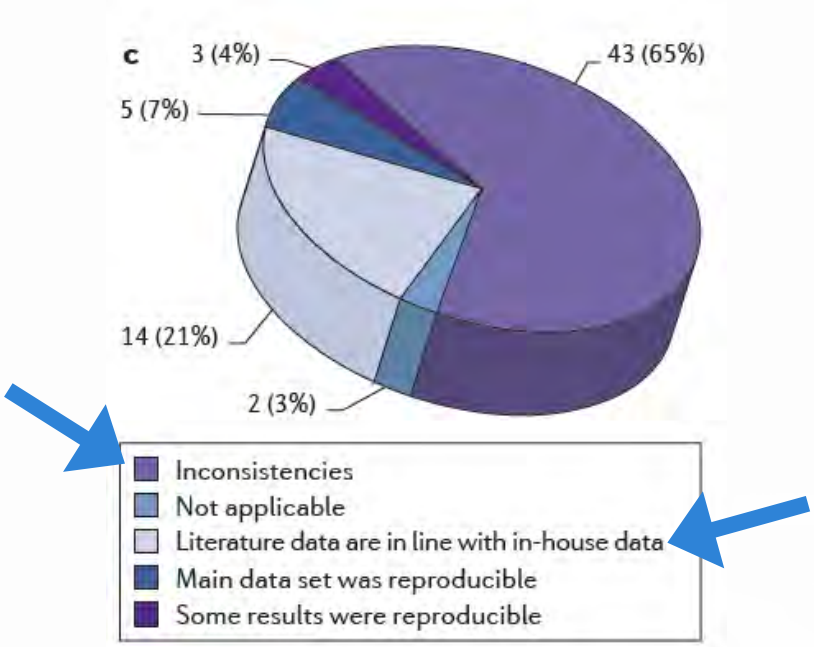
*Paul et. al, *Nature Rev. Drug Discovery,* March 2010; † Leigh Anderson, *Clin Chem*, 2010

Too Many Papers: Is It Just Overwhelming Literature?

NATURE REVIEWS | DRUG DISCOVERY

Believe it or not: how much can we rely on published data on potential drug targets?





Prinz et. al, *Nature Drug Discovery,* August 2011

Innovation Exists in Public Sector Research Institutions (PSRIs)

Table 1. Number of Drug Products Approved by the Food and Drug Administration and Originating from Public-Sector Research, According to Therapeutic Area, 1970–2009.

Therapeutic Area	Number
Total	153
Hematology or oncology	40
Infectious disease	36
Cardiology	12
Metabolic disease	12
Central nervous system	12
Dermatology	7
Renal disease	7
Ophthalmology	6
Immunology	6
Gastroenterology	4
Women's health	3
Allergy	2
Pulmonary disease	2
Urology	2
Anesthesiology	1
Dental disorders	1

Table 2. FDA-Approved Drugs Discovered through Public-Sector Research, According to Type of Review and Chemical Type, 1990–2007.*

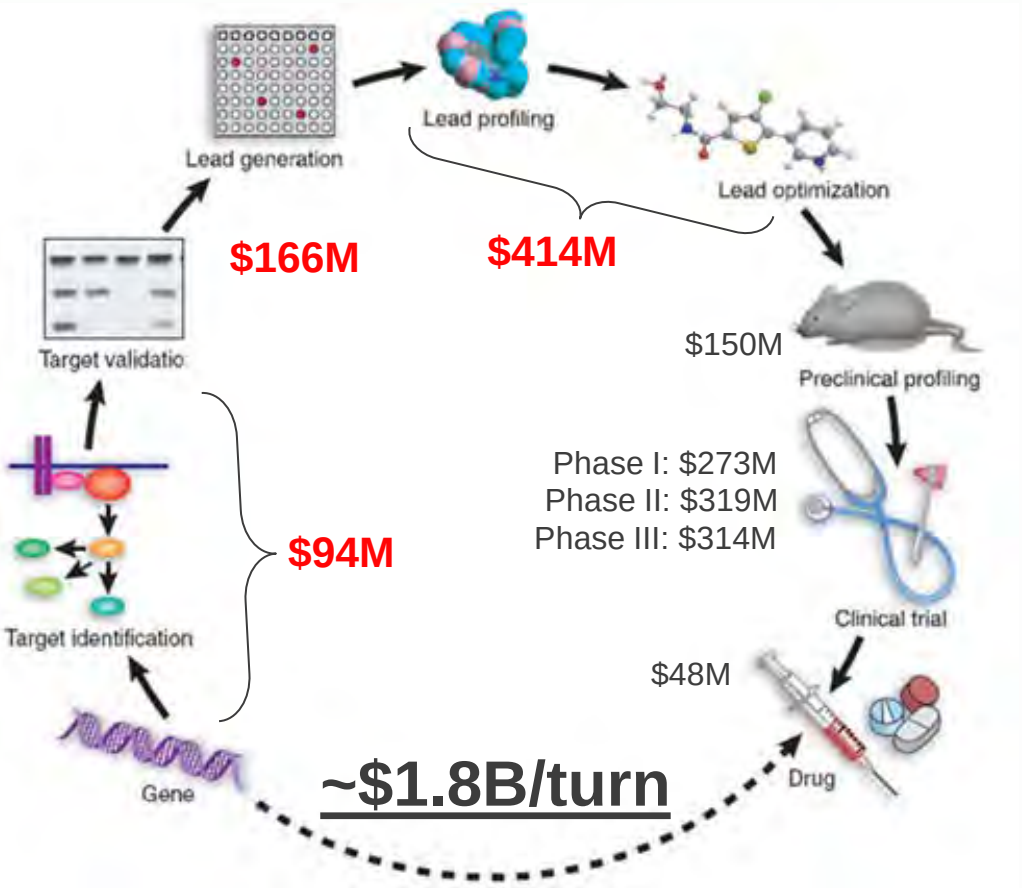
Type of Review	New Molecular Entity	New Ester, Salt, or Derivative	New Formulation	New Combination	New Manufacturer	New Indication	Already Marketed	Total
Priority review								
Discovered by PSRI (no.)	44	1	17	3	0	1†	0	66
All FDA approvals (no.)	209	6	99	20	14	0	0	348
Rate of PSRI discovery (%)	21.1	16.7	17.2	15.0	0	NA	NA	19.0
Standard review								
Discovered by PSRI (no.)	20	0	36	6	7	8	0	77
All FDA approvals (no.)	274	33	631	96	137	10	12	1193
Rate of PSRI discovery (%)	7.3	0	5.7	6.3	5.1	80.0	0	6.5
All approvals								
Discovered by PSRI (no.)	64	1	53	9	7	9	0	143
All FDA approvals (no.)	483	39	730	116	151	10	12	1541
Rate of PSRI discovery (%)	13.3	2.6	7.3	7.8	4.6	90.0	0	9.3

Over the past 40 years,

- **153** FDA approvals were carried out in PSRIs (~9.3% of overall approvals)
  - 93 small molecule
  - 36 biologics
  - 15 vaccines
  - 8 IVDs
  - 1 over-the-counter drug
- Most prolific PSRIs include:
  - NIH (22 products)
  - UC system (11 products)
  - MSKCC (8 products)
  - Emory (7 products)
  - Yale (6 products)
- Virtually all important, innovative vaccines that have been introduced in the last 25 years have been created by PSRIs

Stevens et. al, *New England Journal of Medicine*, Feb 2011

Translation Pace: How To Break Out of Current Paradigm?



Turning the Crank…

Key Needs (from community '02)

- Standards and protocols
- Real-time, public release of data
- Large, multi-disciplinary teams
- Pilot-friendly team environment to share failures and successes
- Team members with **trans-disciplinary training**

The potential to transform cancer drug discovery and diagnostics

Paul et. al, *Nature Rev. Drug Discovery,* March 2010

National Cancer Program: Stakeholders

Center for Strategic Scientific Initiatives

~$18 B per year

National Cancer Institute

NCAB Working Group Report, 2010

National Cancer Institute Organization

Director
Harold Varmus, MD

National Cancer Institute

$5.07B

(FY12)

Deputy Director
Douglas Lowy, MD

Office of the Director

CSSI **CCG**

~$190 M (~4%)

Center for Cancer Research

Division of Cancer Epidemiology and Genetics

Division of Cancer Treatment and Diagnosis

Division of Cancer Biology

Division of Cancer Control and Population Sciences

Division of Cancer Prevention

Division of Extramural Activities

Conducting – Intramural

Funding – Extramural

NCI Center for Strategic Scientific Initiatives (CSSI): Concept Shop

Director
Douglas Lowy, MD

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

~$190M (FY12)

Deputy Director
Jerry S.H. Lee, PhD

Office of Cancer Clinical Proteomics Research

Director
Henry Rodriguez, PhD, MBA

Office of Physical Sciences-Oncology

Director
Larry A. Nagahara, PhD

Office of Cancer Nanotechnology Research

Director
Piotr Grodzinski, PhD

Office of Cancer Genomics

Director
Daniela S. Gerhard, PhD

The Cancer Genome Atlas Program Office

Director
Kenna M.Shaw, PhD

*Center for Cancer Genomics (CCG) shown in yellow

NCI Center for Strategic Scientific Initiatives (CSSI): Concept Shop

Director
Douglas Lowy, MD

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

~$190M (FY12)

Deputy Director
Jerry S.H. Lee, PhD

Mission

"…to create and uniquely implement exploratory programs focused on the development and integration of advanced technologies, **trans-disciplinary approaches, infrastructures, and standards**, to accelerate the **creation and broad deployment** of **data, knowledge, and tools** to empower the **entire cancer research continuum** in better understanding and leveraging knowledge of the cancer biology space **for patient benefit**…"

IMAT Innovative Molecular Analysis Technologies

2003, 2007, 2011

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

2005, 2010

PHYSICAL SCIENCES in ONCOLOGY

2008

Provocative Questions Project

2011

NCI Alliance for Nanotechnology in Cancer

2004, 2008

THE CANCER GENOME ATLAS

2005, 2008

Cancer Target Discovery & Development (CTD²)

2010

Example #1: Cancer Genomics- Taking a Page from Engineers

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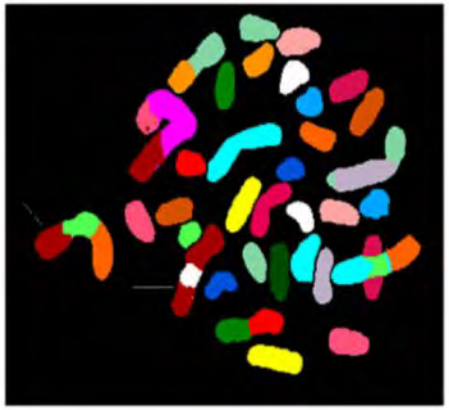
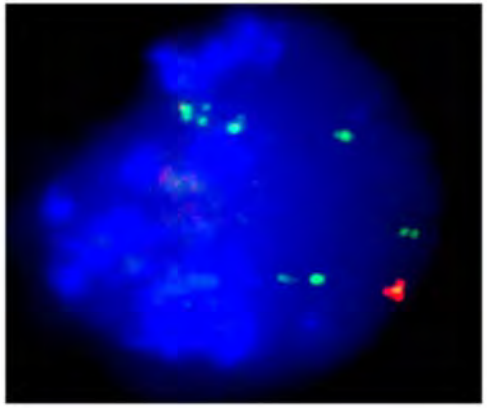
Disease of Genomic Alterations

- Copy number
- Expression (regulation of)
- Regulation of translation
- Mutations
- Epigenome





- **Systematic identification of all genomic changes**
- **Repeat (a lot) for individual cancer**
- **Repeat for many cancers**
- **Make it publically available**

	Saturated steam			Superheated steam		
Pressure (kg/cm^2)	Temp (°C)	Vapour enthalpy (kcal/kg)	Specific volume (m^3/kg)	Density (kg/m^3)	Specific volume (m^3/kg) at 250°C	Specific volume (m^3/kg) at 300°C
1	99,1	638.8	1,725	0,580	2,454	2,691
2	119,6	646.2	0,902	1,109	1,223	1,342
3	132,9	650.6	0,617	1,621	0,812	0,893
4	142,9	653,7	0,471	2,123	0,607	0,668
5	151,1	656.0	0,382	2,618	0,484	0,533
6	158,1	657.0	0,321	3,115	0,402	0,443
7	164,2	659,5	0,278	3,597	0,343	0,379
8	169,6	660.8	0,245	4,082	0,299	0,331
9	174,5	661.9	0,219	4,566	0,265	0,293
10	179,1	662.9	0,198	5,051	0,238	0,263
12	187,1	664.5	0,166	6,024	0,196	0,218
14	194,1	665,7	0,143	6,993	0,167	0,186
16	200,4	666.7	0,126	7,937	0,145	0,162
18	206,1	667,4	0,112	8,929	0,128	0,143
20	211,4	668.0	0,101	9,901	0,114	0,128
22	216,2	668.4	0,092	10.870	0,103	0,116
24	220,7	668.7	0,085	11.765	0,093	0,106
26	225,0	669,0	0,078	12,821	0,085	0,097
28	229,0	669,1	0,073	13.699	0,078	0,089
30	232,7	669.2	0,068	14.706	0,072	0,083

Steam table (Reference)

Many “Thermometers”: Heterogeneity of Platforms

454

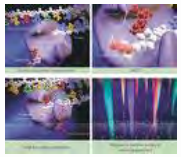
Illumina

SOLiD

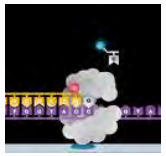
Complete Genomics

Complete Genomics

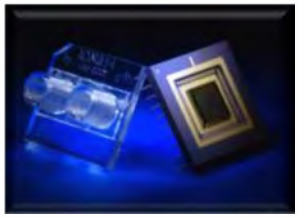
Helicos



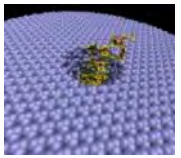
Visigen



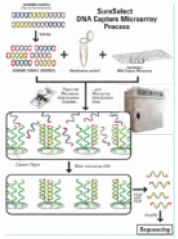
PacBio



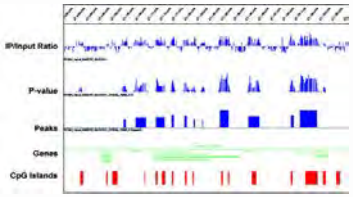
Ion-Torrent



Oxford Molecular



Agilent

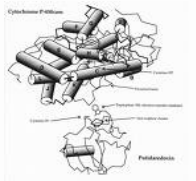


Nimblegen

LaserGen, Inc.

LaserGen

ZSGenetics



NABsys

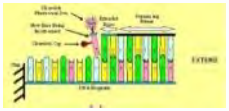
NABsys

(Sponsoring the CNF Annual Meeting and the Poster Session Awards)

Raindance

febit

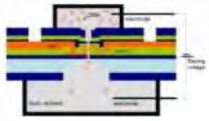
Febit



Intelligent Biosystems

Halycon

IBM



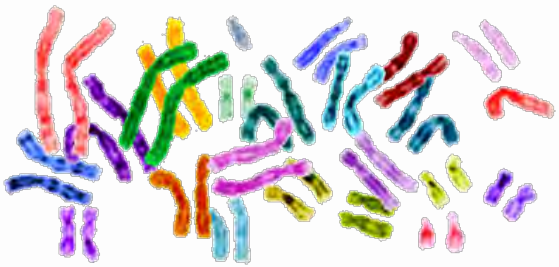
Key Innovation:
Samples AND Handling Matter!

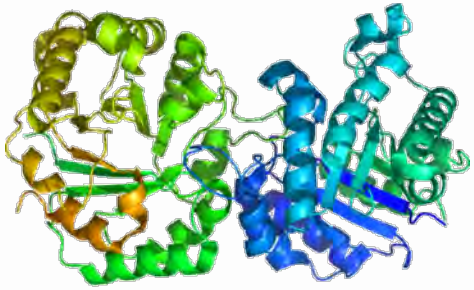
caHUB The Cancer Human Biobank

Center for Strategic Scientific Initiatives

Genomics

Proteomics





All Depend On High-Quality, Annotated Human Biospecimens

"Garbage In…Garbage Out"

National Cancer Institute

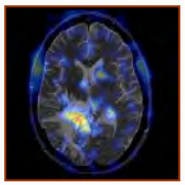
TCGA: Connecting Multiple Standardized Sources, Experiments, and Data Types

Center for STRATEGIC Scientific Initiatives

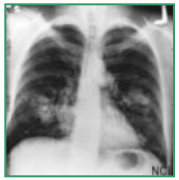
The Cancer Genome Atlas

Three Cancers- Pilot

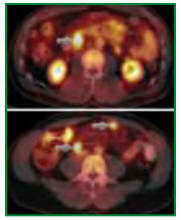
glioblastoma multiforme (brain)



squamous carcinoma (lung)



serous cystadenocarcinoma (ovarian)



Biospecimen Core Resource with more than 13 Tissue Source Sites

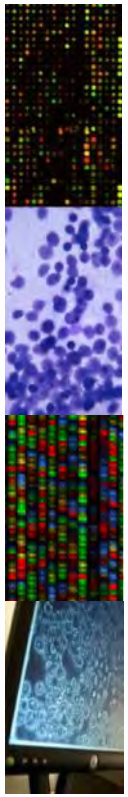
7 Cancer Genomic Characterization Centers

3 Genome Sequencing Centers

Data Coordinating Center

Multiple data types

- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence

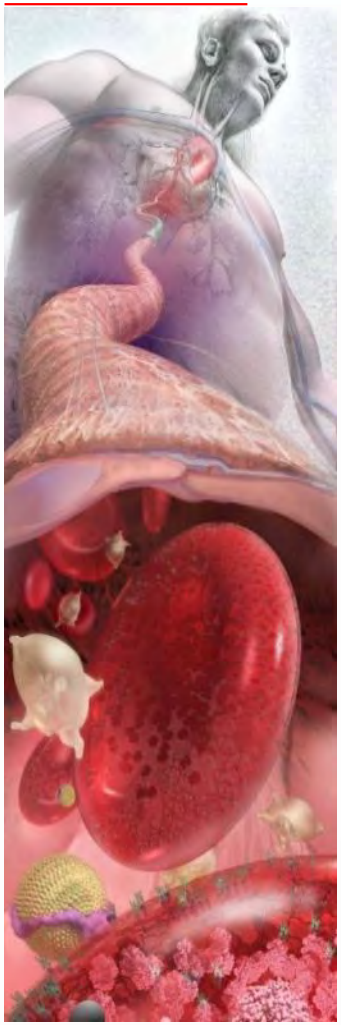


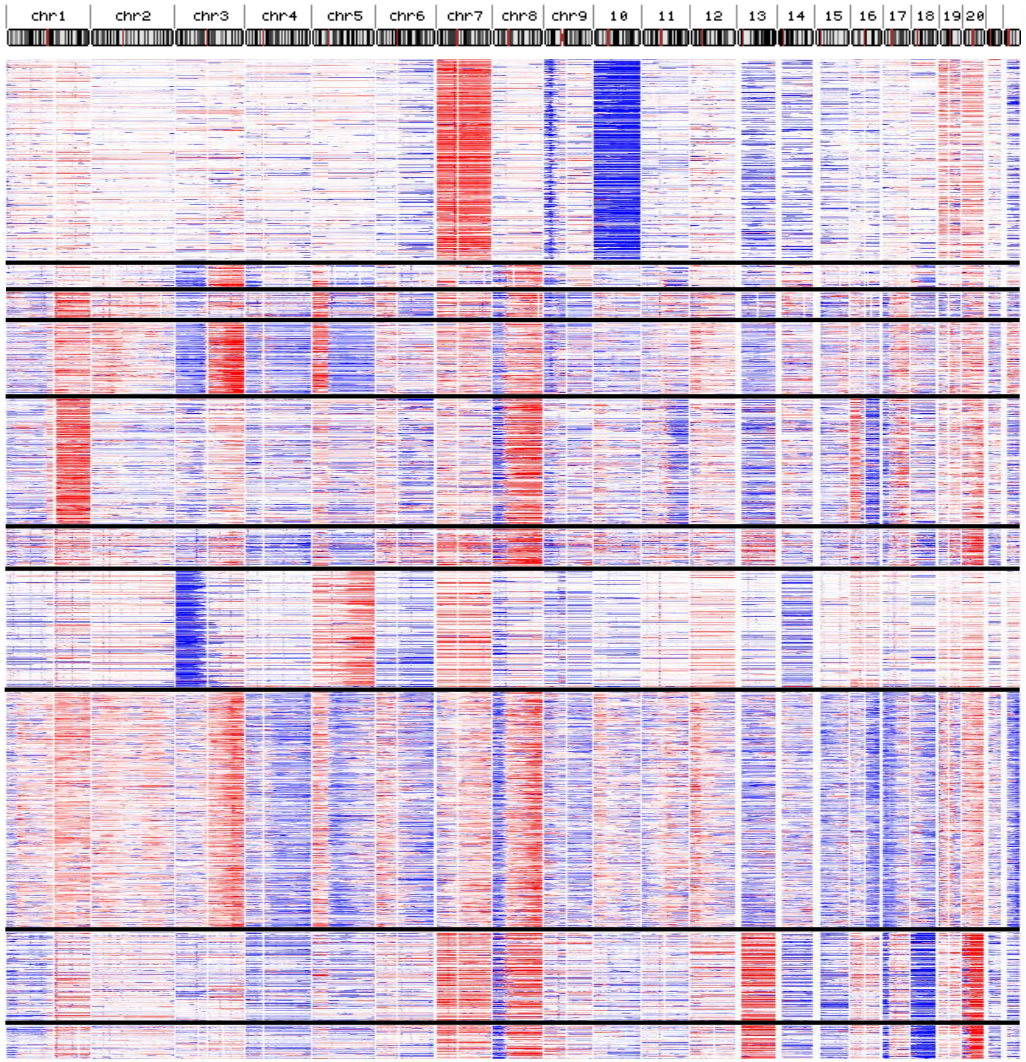
Genomic "Steam Table"

The Cancer Genome Atlas Data Portal — Understanding genomics to improve cancer care

Center for Strategic Scientific Initiatives

Summer 2011





Glioblastoma:	470
Head & neck:	51
Lung adeno:	57
Lung squamous:	159
Breast carcinoma:	180
Stomach adeno:	84
Kidney clear carc:	260
Ovarian serous:	520
Colon adeno:	198
Rectum carcinoma:	
Total:	

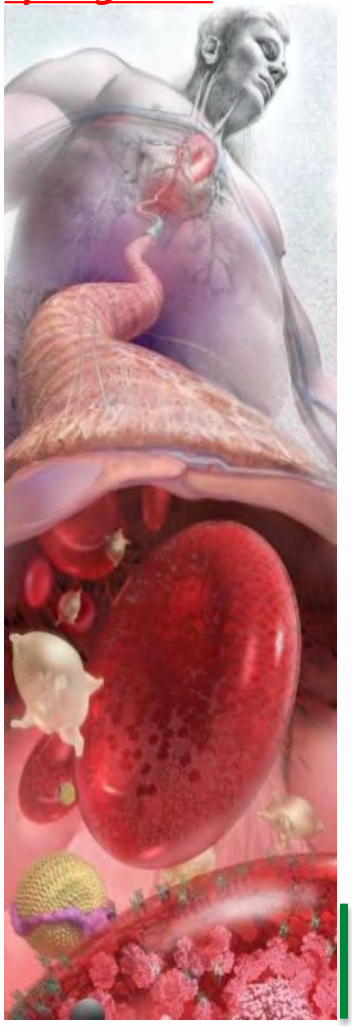
Source: UCSC Cancer Genomic Heatmaps (CopyNumber SNP6)
[https://genome-cancer.ucsc.edu/] Compiled by Jerry S.H. Lee, PhD, May 2011

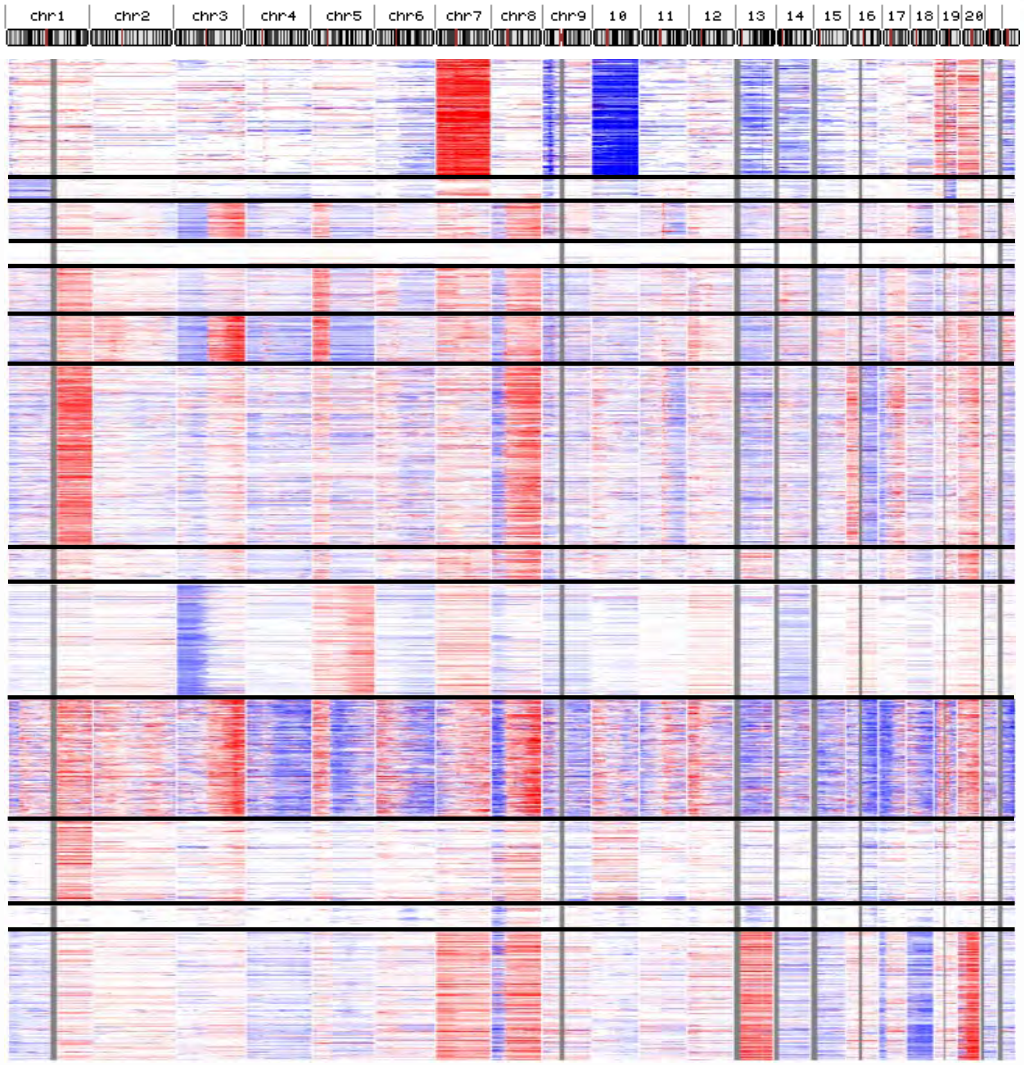
Genomic "Steam Table"

The Cancer Genome Atlas Data Portal — Understanding genomics to improve cancer care

Center for Strategic Scientific Initiatives

Spring 2012





Glioblastoma:	535
Brain lower grade glioma:	80
Head & neck:	165
Thyroid carcinoma:	85
Lung adeno:	205
Lung squamous:	211
Breast carcinoma:	783
Stomach adeno:	149
Kidney clear carc:	489
Ovarian serous:	520
Uterine corpus end. car.:	363
Prostate adenocarcinoma:	82
Colon/rectum adeno:	564
Total:	

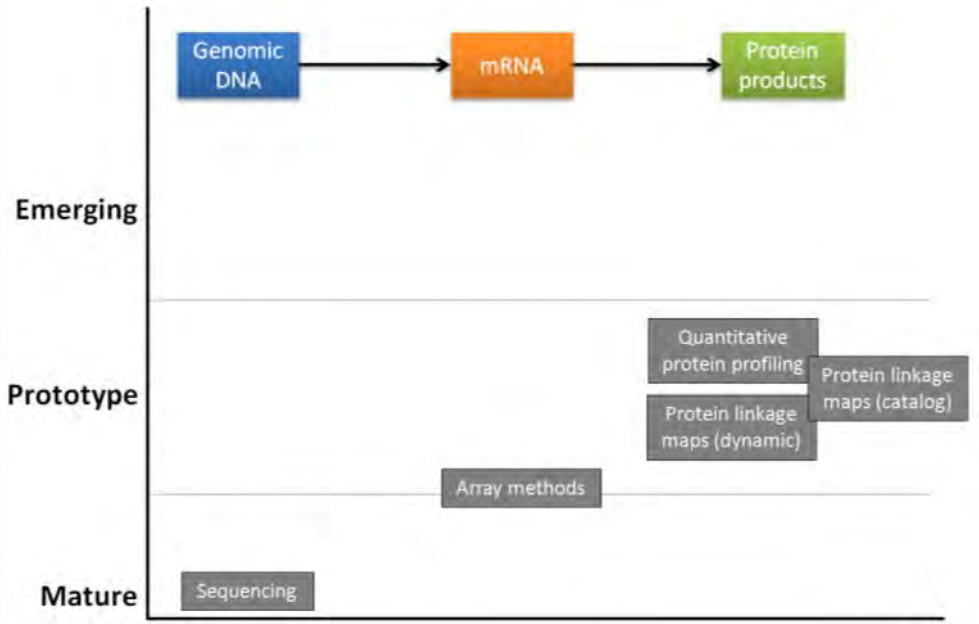
Source: UCSC Cancer Genomic Heatmaps (CopyNumber GISTIC2)
[https://genome-cancer.ucsc.edu/] Compiled by Jerry S.H. Lee, PhD, Feb 2012

Example #2: Cancer Proteomics and Mass Spectrometry

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

Technologies for Quantitative Analysis



Major Challenges

- Analytical variability in platforms
- Lack of standards, protocols, and reference data
- No consensus on data acquisition, analysis, and open access reporting of raw data

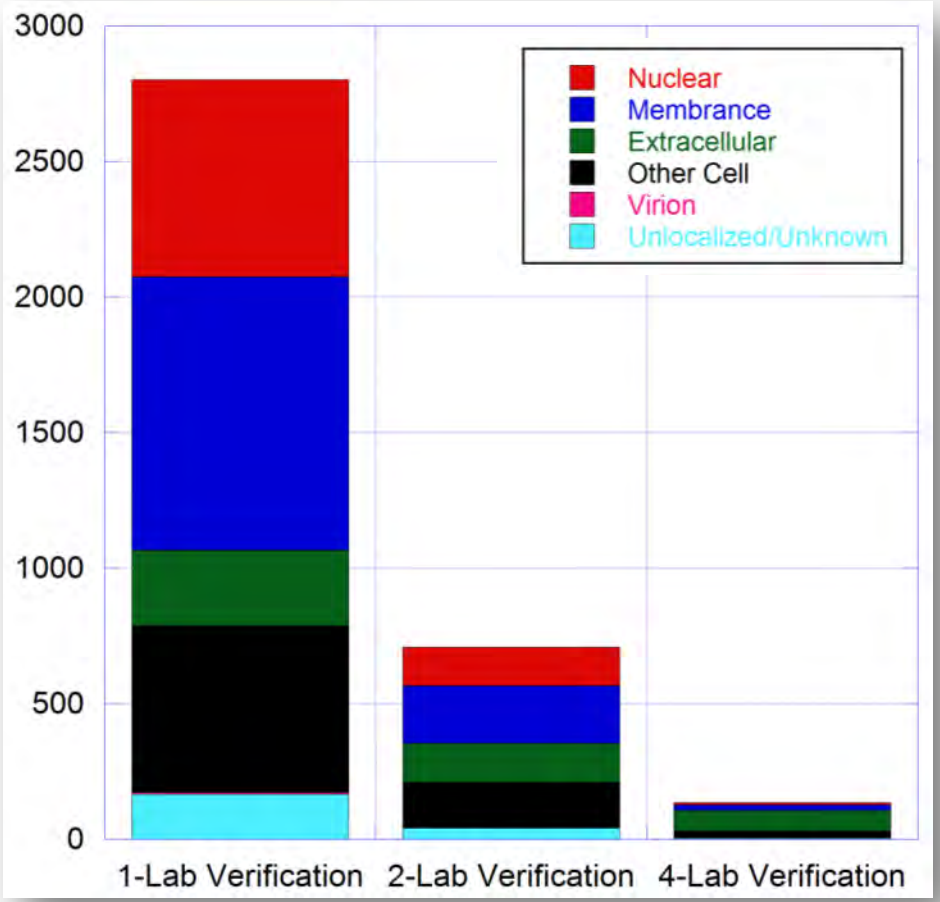
Unlike genomic technologies, proteomic technologies were not yet fully mature

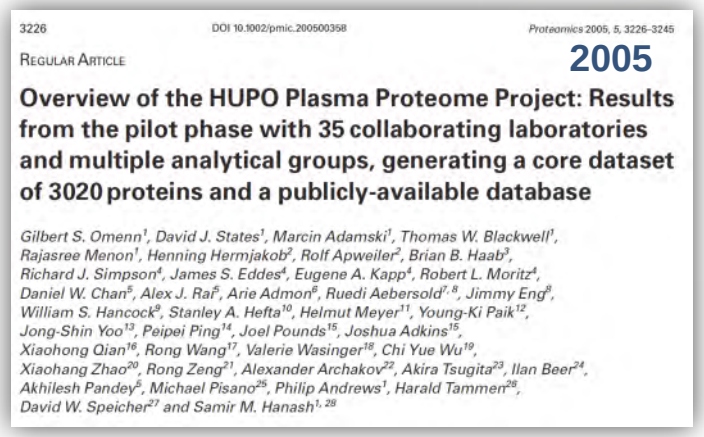
Source: Adopted from "Defining the Mandate of Proteomics in the Post-Genomics Era: Workshop Report." *National Academy of Sciences.* 2002.

Heterogeneity of Platforms and Reproducibility Challenges

Reproducibility of Clinical Proteomics in 2005

CENTER for STRATEGIC SCIENTIFIC INITIATIVES





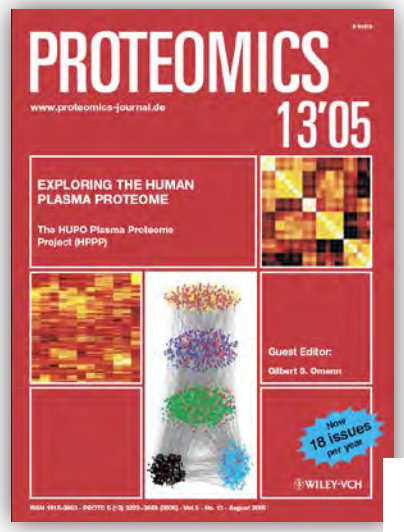
3226 DOI 10.1002/pmic.200500358 *Proteomics* 2005, 5, 3226–3245

REGULAR ARTICLE

2005

Overview of the HUPO Plasma Proteome Project: Results from the pilot phase with 35 collaborating laboratories and multiple analytical groups, generating a core dataset of 3020 proteins and a publicly-available database

Gilbert S. Omenn[1], David J. States[1], Marcin Adamski[1], Thomas W. Blackwell[1], Rajasree Menon[1], Henning Hermjakob[2], Rolf Apweiler[2], Brian B. Haab[3], Richard J. Simpson[4], James S. Eddes[4], Eugene A. Kapp[4], Robert L. Moritz[4], Daniel W. Chan[5], Alex J. Rai[5], Arie Admon[6], Ruedi Aebersold[7, 8], Jimmy Eng[8], William S. Hancock[9], Stanley A. Hefta[10], Helmut Meyer[11], Young-Ki Paik[12], Jong-Shin Yoo[13], Peipei Ping[14], Joel Pounds[15], Joshua Adkins[15], Xiaohong Qian[16], Rong Wang[17], Valerie Wasinger[18], Chi Yue Wu[19], Xiaohang Zhao[20], Rong Zeng[21], Alexander Archakov[22], Akira Tsugita[23], Ilan Beer[24], Akhilesh Pandey[3], Michael Pisano[25], Philip Andrews[1], Harald Tammen[26], David W. Speicher[27] and Samir M. Hanash[1, 28]



Courtesy of Gil Omenn

Clinical Proteomic Technologies for Cancer (CPTAC) Pilot

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

nature biotechnology

Multi-site assessment of the precision and reproducibility of multiple reaction monitoring–based measurements of proteins in plasma

Reproducibility

- **First demonstration** that MRM is highly reproducible **across multiple laboratories** and technology platforms
- **Community Resource**: Antibody Characterization Laboratory Launched

Data Sharing ("Amsterdam Principles")

- **Timing**
  - Data generated by individual investigators should **be released into the public domain at the latest upon publication while data generated by community resource projects should be released upon generation** following appropriate QA/QC procedures
- **Comprehensiveness**
  - High quality raw data (e.g., mass spectral, protein/affinity array data) be released to the public. They should be well annotated with metadata, information on data quality, and identification quality control data
- **Format**
  - Open access to proteomic data requires community-supported standardized formats, controlled vocabularies, reasonable reporting requirements, and publicly available central repositories

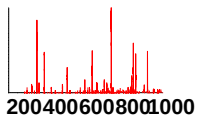
research articles Journal of proteome research

May 2009

Recommendations from the 2008 International Meeting on Proteomics Data Release and Sharing Policy: The Amsterdam Principles

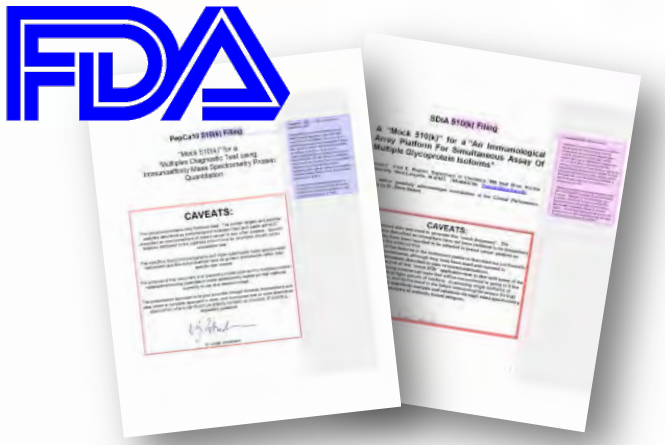
Henry Rodriguez,*,† Mike Snyder,‡ Mathias Uhlén,§ Phil Andrews,|| Ronald Beavis,⊥ Christoph Borchers,# Robert J. Chalkley,∇ Sang Yun Cho,○ Katie Cottingham,◆ Michael Dunn,¶ Tomasz Dylag,† Ron Edgar,□ Peter Hare,■ Albert J. R. Heck,● Roland F. Hirsch,▼ Karen Kennedy,○ Patrik Kolar,† Hans-Joachim Kraus,● Parag Mallick,□ Alexey Nesvizhskii,● Peipei Ping,□ Fredrik Pontén,▼ Liming Yang,◆ John R. Yates,○ Stephen E. Stein,□ Henning Hermjakob,● Christopher R. Kinsinger,† and Rolf Apweiler●

Center for Strategic Scientific Initiatives, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, 20892, Department of Molecular, Cellular, and Developmental Biology, Yale University, New Haven, Connecticut 06520, KTH Biotechnology, KTH - AlbaNova University Center, Stockholm, Sweden, Department of Biological Chemistry, University of Michigan Medical School, Ann Arbor, Michigan 48109, Department of Medical Genetics, University of British Columbia, Vancouver, British Columbia, Canada, University of Victoria Proteomics Centre, Victoria, British Columbia, Canada, Department of Pharmaceutical Chemistry, University of California, San Francisco, San Francisco, California, 94158, Yonsei Proteome Research Center, Yonsei



CPTAC Pilot: Crosstalk with FDA and Educating Community

- **Analytical Validation Review Documents**
  - CPTAC/FDA Workshop - identify analytical validation needs for clinical proteomic technologies in the context of intended use



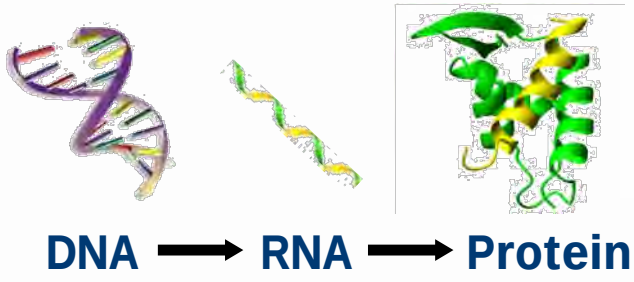
- **Outputs:**
  - Public mock 510(k) pre-applications that serve as review documents on:
    - multiplex MRM-MS assay
    - multiplex affinity-based assay
  - Published in special issue of *Clinical Chemistry* (by AACC), that informs research community and FDA to technology platforms that will likely be part of future 510k submissions

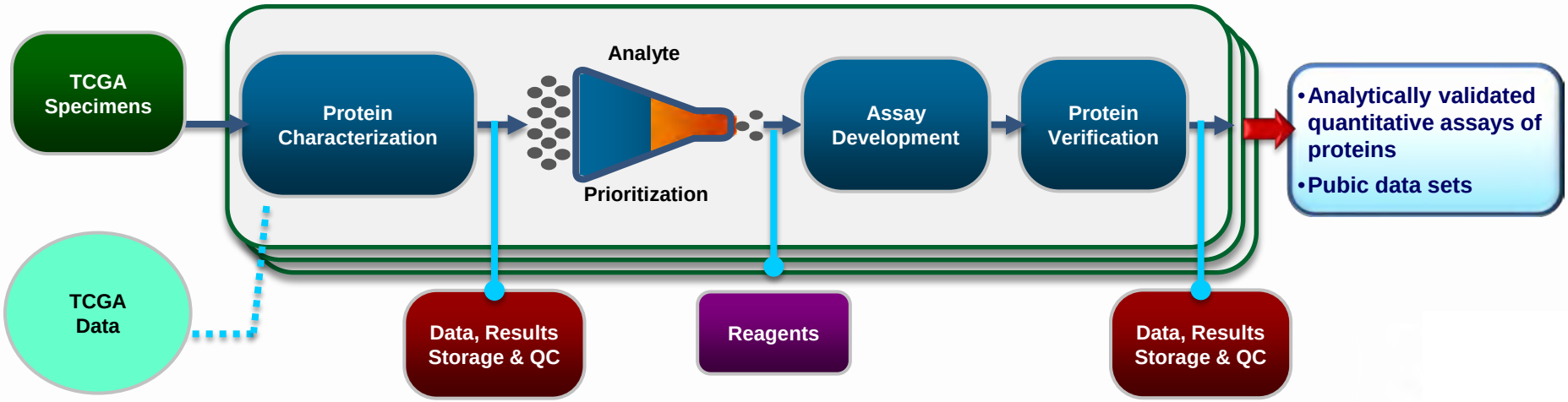
Clinical Proteomic Tumor Analysis Centers (CPTAC Phase II)

Center for STRATEGIC Scientific Initiatives

Phase II Launched Sept 2011

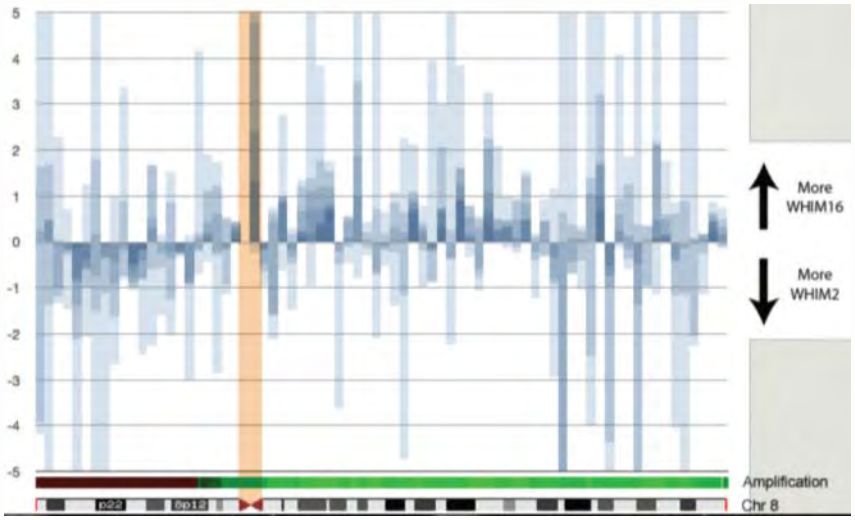
- Analyze matched TCGA samples using two approaches
  - Targeting genome to proteome
  - Mapping proteome to genome
- Develop validated and quantitative assays and reagents
- Distribute raw and analyzed data via public data portal





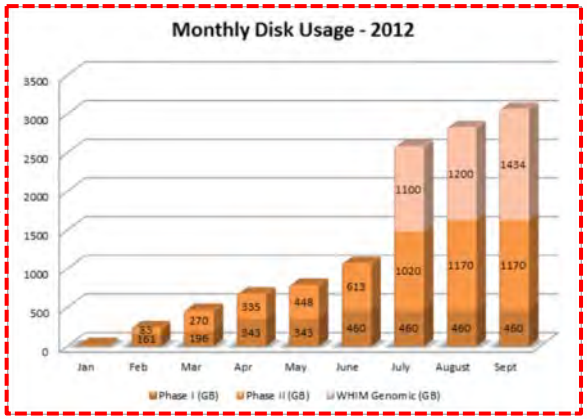
CPTAC Phase II: Highlights, Progress to Date, and Data Release

Status Update: Fall 2012



Chr 8

- **Due diligence studies** near completion
  - Cross network experiments show comparable lab-to-lab measurements
- **Orthogonal** proteomic platforms and analysis (proteome → genome vs. genome → proteome) reveal **additional unexpected complexities**
- Verifying new insights will require **additional sample sets** and **development of novel analysis** algorithms and techniques
- Public data portal access **OPEN!** (Phase I: 351 GB, Phase II: 616 GB)



Where Do We Go From Here?
Is it JUST More Data?

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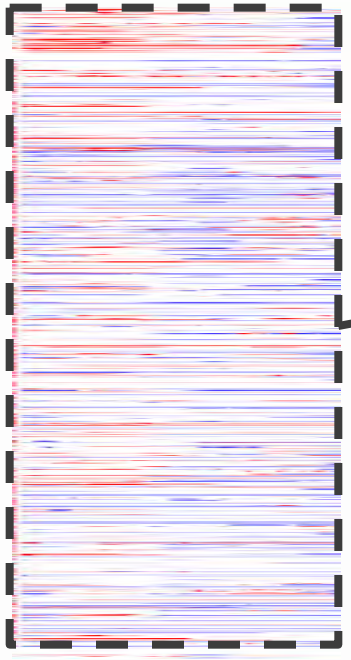
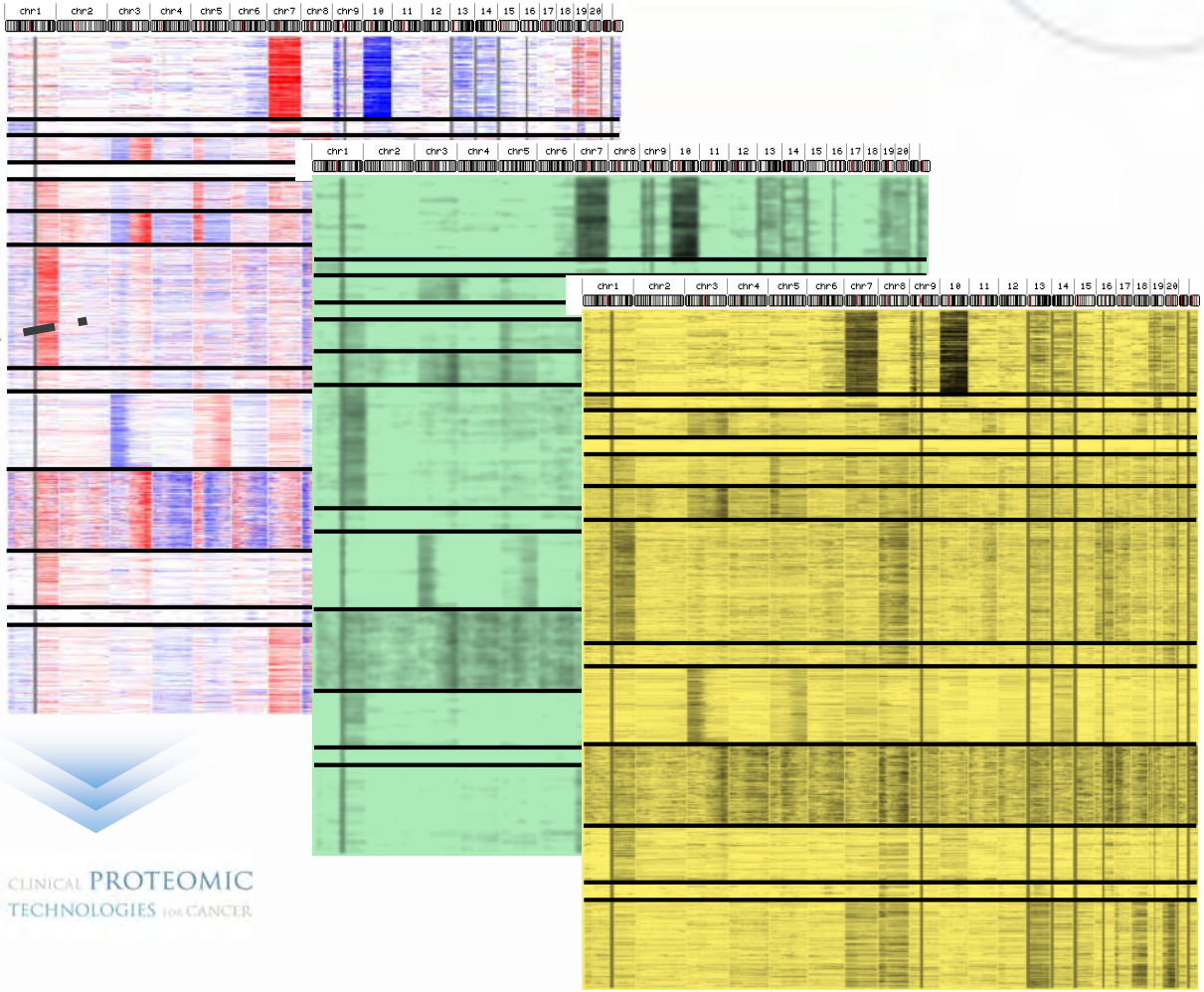


Physics?

PHYSICAL SCIENCES in ONCOLOGY

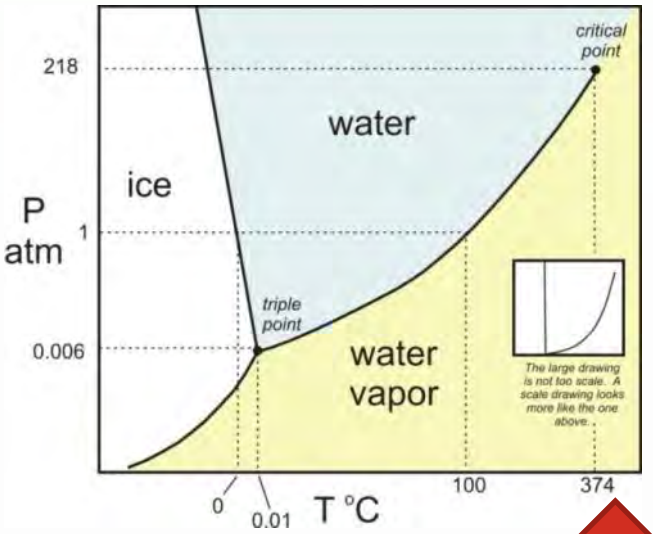


CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Time? (Evolution)

Standards and Sharing of Data → New Insights and Understanding

- Define *samples & protocols*
  - ***Share collected data***



New Understanding

- **Phase boundaries**
  - V/L equilibrium
  - **Triple Point**

(Phase Diagram)

New Parameter

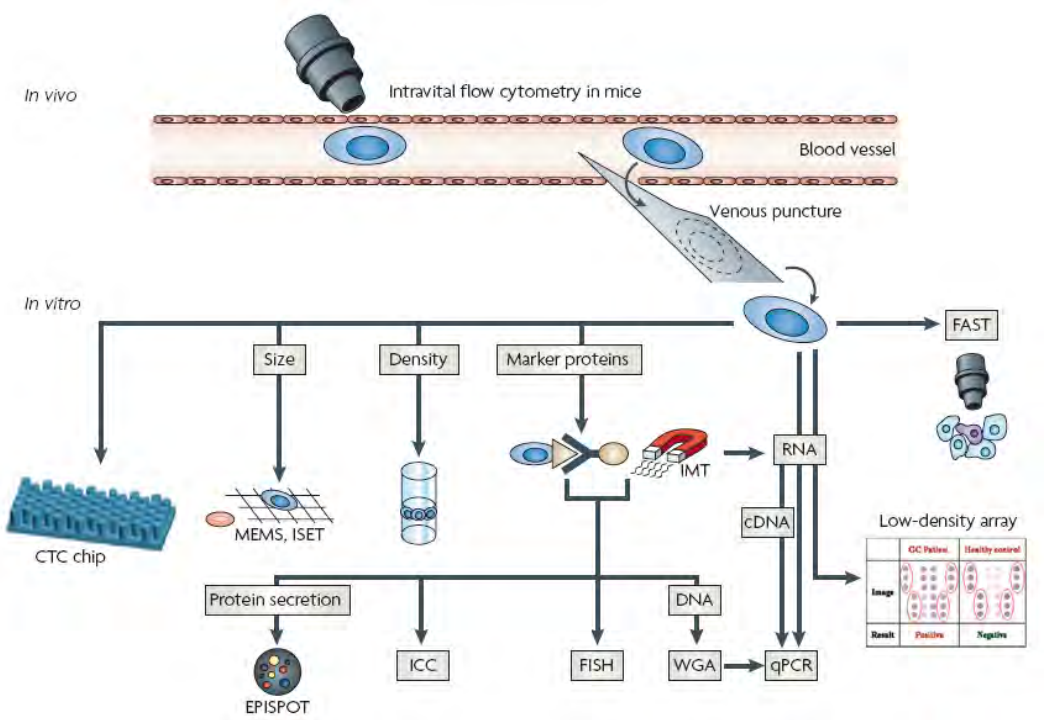
"Pressure"

Saturated steam					Superheated steam	
Pressure (kg/cm²)	Temp (°C)	Vapour enthalpy (kcal/kg)	Specific volume (m³/kg)	Density (kg/m³)	Specific volume (m³/kg) at 250°C	at 300°C
1	99,1	638,8	1,725	0,580	2,454	2,691
2	119,6	646,2	0,902	1,109	1,223	1,342
3	132,9	650,6	0,617	1,621	0,812	0,893
4	142,9	653,7	0,471	2,123	0,607	0,668
5	151,1	656,0	0,382	2,618	0,484	0,533
6	158,1	657,0	0,321	3,115	0,402	0,443
7	164,2	659,5	0,278	3,597	0,343	0,379
8	169,6	660,8	0,245	4,082	0,299	0,331
9	174,5	661,9	0,219	4,566	0,265	0,293
10	179,1	662,9	0,198	5,051	0,238	0,263
12	187,1	664,5	0,166	6,024	0,196	0,218
14	194,1	665,7	0,143	6,993	0,167	0,186
16	200,4	666,7	0,126	7,937	0,145	0,162
18	206,1	667,4	0,112	8,929	0,128	0,143
20	211,4	668,0	0,101	9,901	0,114	0,128
22	216,2	668,4	0,092	10,870	0,103	0,116
24	220,7	668,7	0,085	11,765	0,093	0,106
26	225,0	669,0	0,078	12,821	0,085	0,097
28	229,0	669,1	0,073	13,699	0,078	0,089
30	232,7	669,2	0,068	14,706	0,072	0,083

LOTS of Quantitative and Reproducible Data

(Steam Table)

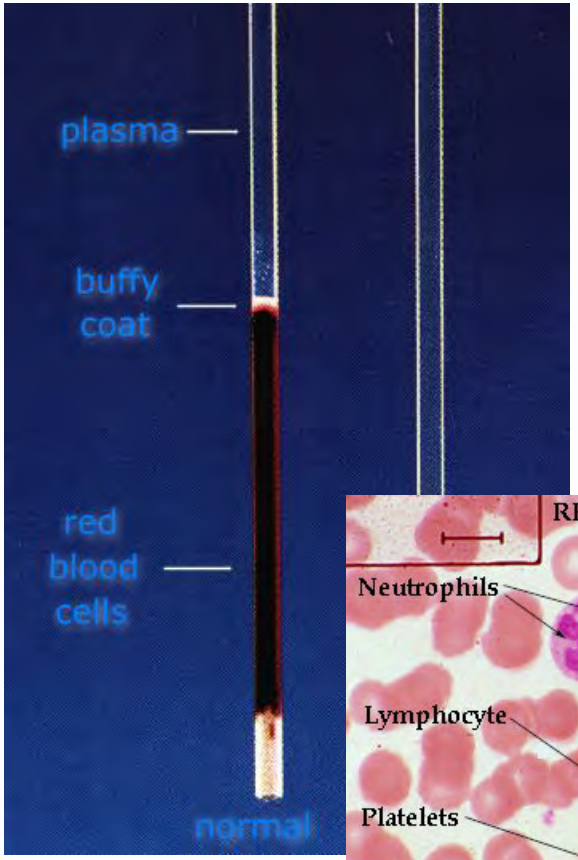
Your Dilemma: Finding the "needle"?

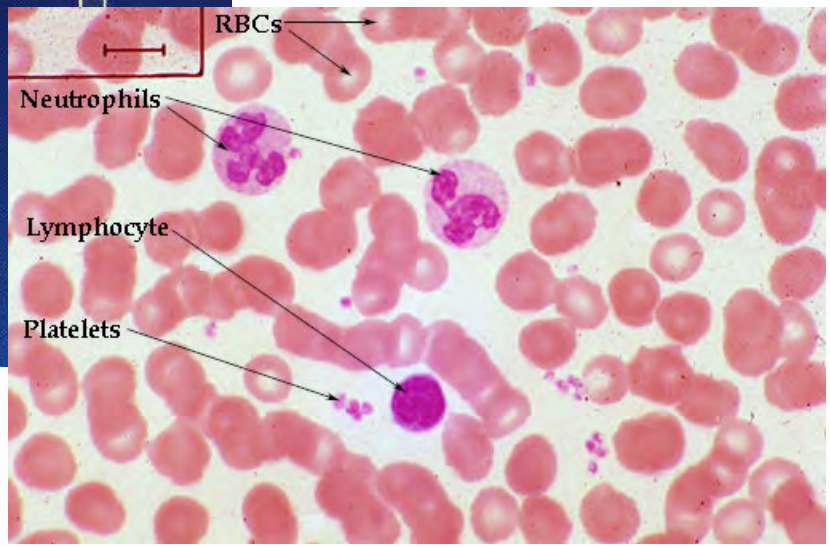


- Understanding of tumor cells in the blood has gained considerable attention in recent years, mainly due to advancements in technology
  - **Disseminated tumor cells (DTCs)** in the bone marrow
  - **Circulating tumor cells (CTCs)** in peripheral blood
- ~ **1** DTC/CTC per **10^6 – 10^7** nucleated blood or BM cells

Pantel *et al. Nature Reviews.* May 2008

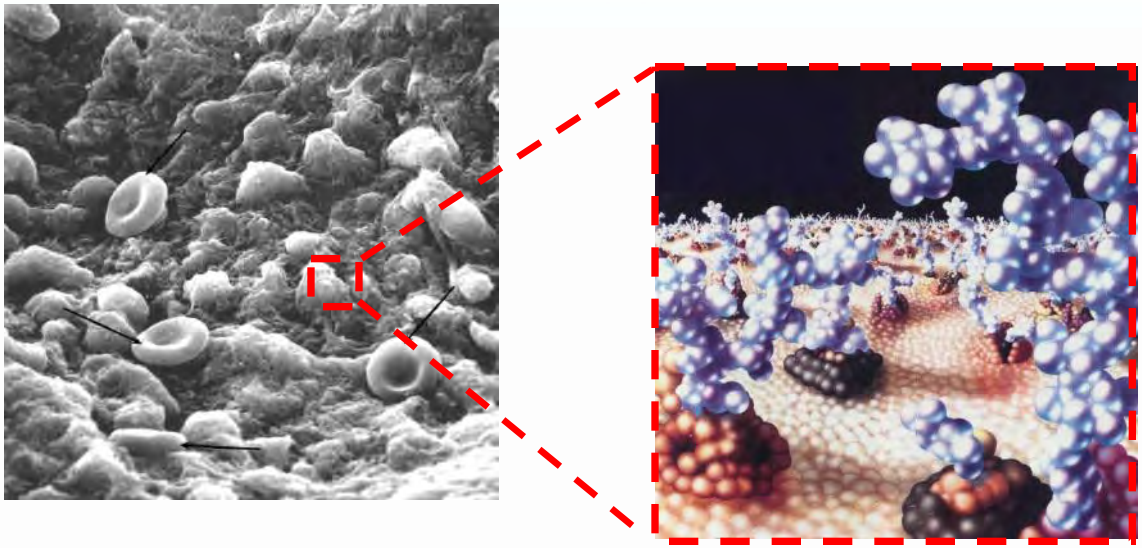
The “hay”: the many components of blood

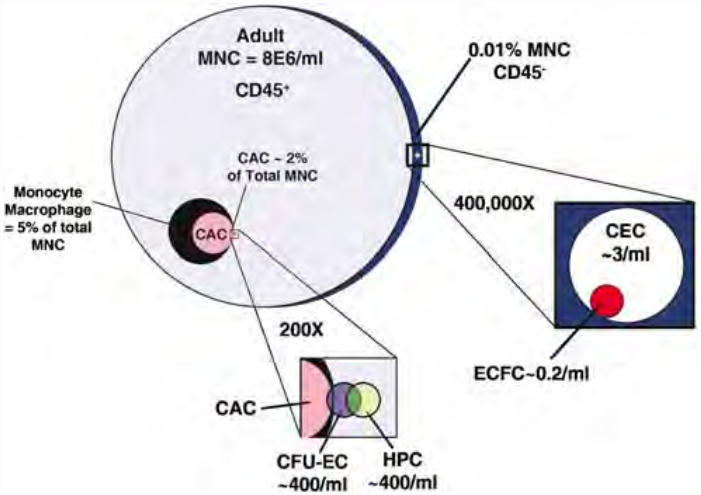




- ~5 liters
- Major elements
  - **~55% Plasma**
    - Mostly water
    - Serum- clotting agents removed
  - **~45% erythrocytes**
    - ~4-6 billion/ml
    - ~2-3 million/second
  - **~1% leukocytes**
    - ~6-10 million/ml
  - **~thrombocytes**
    - ~200-500 million/ml

Sorting out which “needle”





- Finding **A** “needle” is hard enough
- Even harder if there are “decoys” hidden within

Prater *et al. Leukemia.* March 2007

Timing Seems Right…

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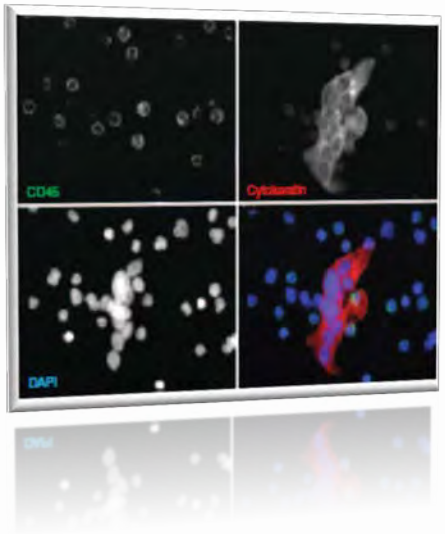
NEWS FEATURE

Beyond counting tumor cells

Since the discovery of circulating tumor cells in 1869, researchers have been able to do little else beyond count them. This is about to change, as advanced technologies for harvesting and analyzing rare cells from blood are opening the window for characterization. Jim Kling reports.

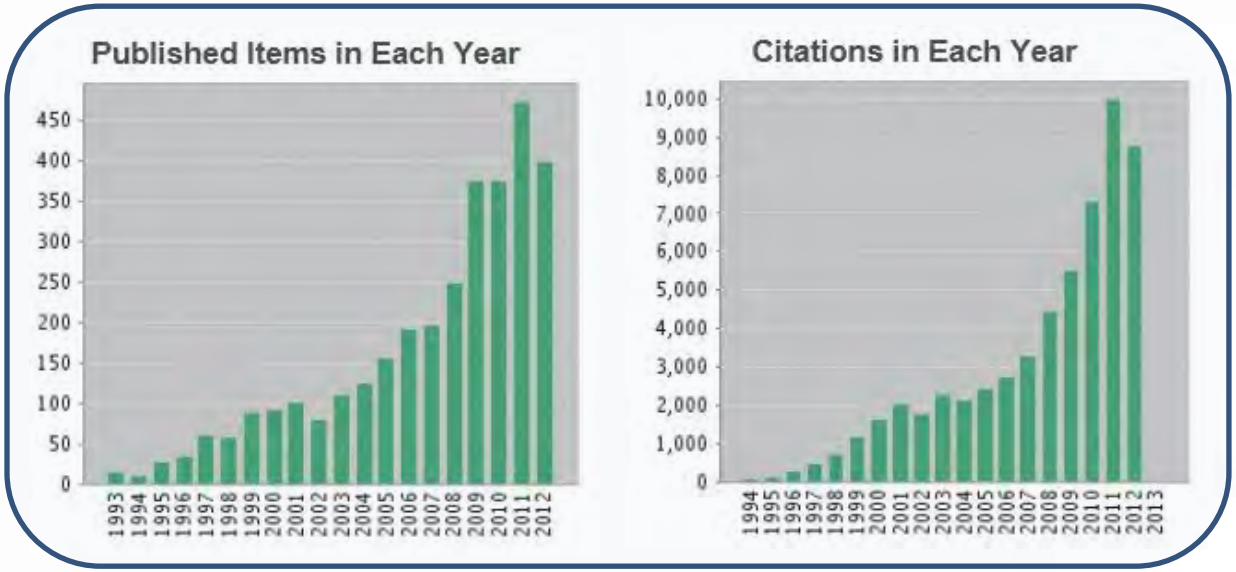


REVIEW

JOURNAL OF TRANSLATIONAL MEDICINE

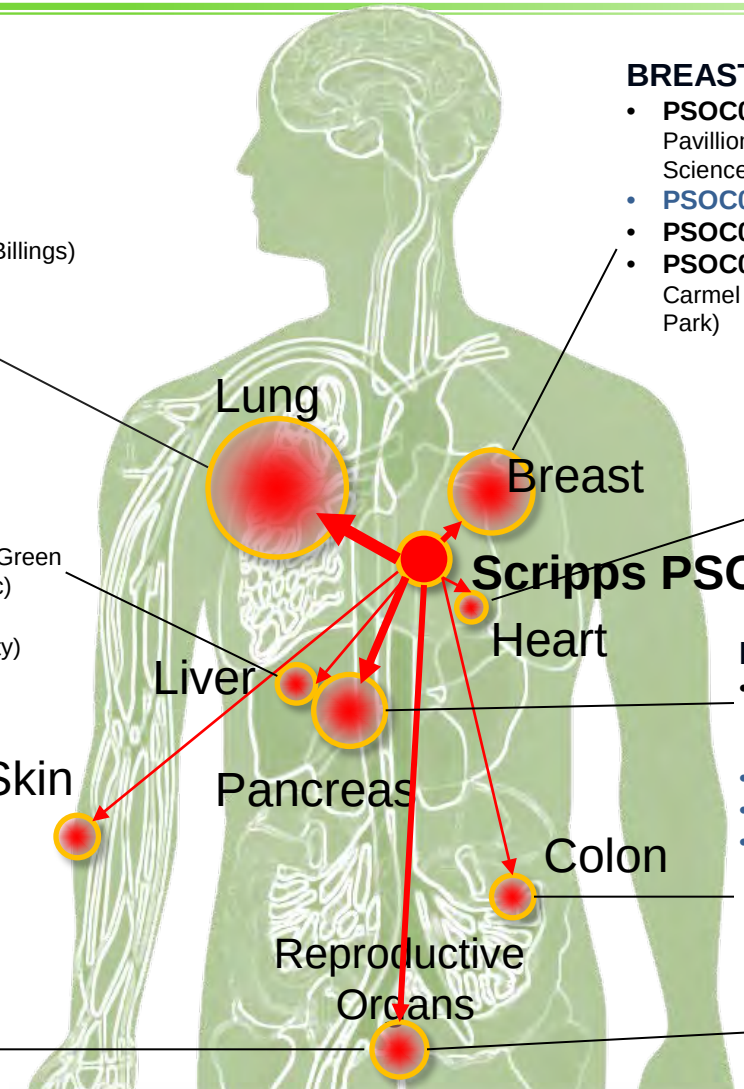
Considerations in the development of circulating tumor cell technology for clinical use

David R Parkinson[1*], Nicholas Dracopoli[2], Brenda Gumbs Petty[3], Carolyn Compton[4], Massimo Cristofanilli[5], Albert Deisseroth[6], Daniel F Hayes[7], Gordon Kapke[8], Prasanna Kumar[9], Jerry SH Lee[10], Minetta C Liu[11], Robert McCormack[12], Stanislaw Mikulski[13], Larry Nagahara[10], Klaus Pantel[14], Sonia Pearson-White[15], Elizabeth A Punnoose[16], Lori T Roadcap[17], Andrew E Schade[18], Howard I Scher[19], Caroline C Sigman[3] and Gary J Kelloff[10]



Statistics generated using *Web of Science* with keywords “circulating tumor cells”

Scripps PSOC Clinical Studies



LUNG:
- **PSOC0043** (UCSD, Billings)
- **PSOC0044** (Scripps Clinic, UCSD, Billings)
- **PSOC0046** (UCSD)
- **PSOC0047** (NKI, UCSD, Billings)
- **PSOC0048** (NKI, Amsterdam)
- **PSOC0049** (Stanford, USC)
- **PSOC0064** (UCSD)
- **PSOC0065** (UCSD)

LIVER:
- **PSOC0050** (Scripps Green Hospital, Scripps Clinic)
- **PSOC0055** (UCSF, Northwestern University)

SKIN:
- **PSOC0056** (Pacific Oncology and Hematology)
- **PSOC0061** (Nevada Cancer Center)

PROSTATE:
- **PSOC0045** (Scripps Clinic: Anderson Outpatient Pavillion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0051** (USC)
- **PSOC0058** (USC)
- **PSOC0060** (Scripps Health)
- **PSOC0063** (NorthShore)

BREAST:
- **PSOC0045** (Scripps Clinic: Anderson Outpatient Pavillion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0053** (Duke University)
- **PSOC0060** (Scripps Health)
- **PSOC0062** (Scripps Clinic: Anderson Outpatient Pavillion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)

HEART:
- **PSOC0057** (Scripps Health)

PANCREAS:
- **PSOC0045** (Scripps Clinic: Anderson Outpatient Pavillion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0054** (UCSF)
- **PSOC0059** (Scripps Green Hospital)
- **PSOC0060** (Scripps Health)

COLON:
- **PSOC0066** (Scripps Clinic)

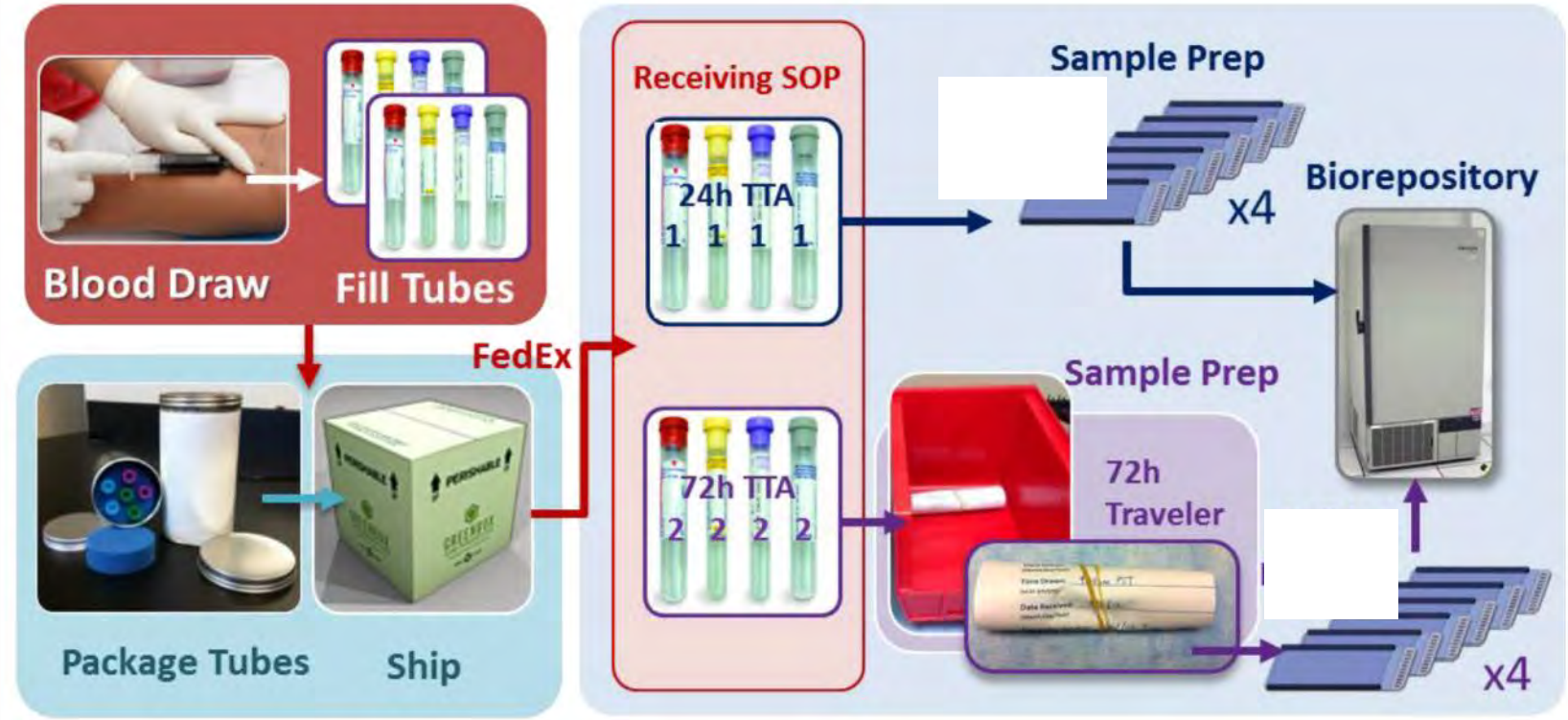
OVARIAN:
- **PSOC0052** (Scripps Memorial Hospital, South Coast Gynecologic Oncology)

Courtesy of Peter Kuhn (TSRI)

Pilot Project: Impact of pre-analytical variables on CTCs

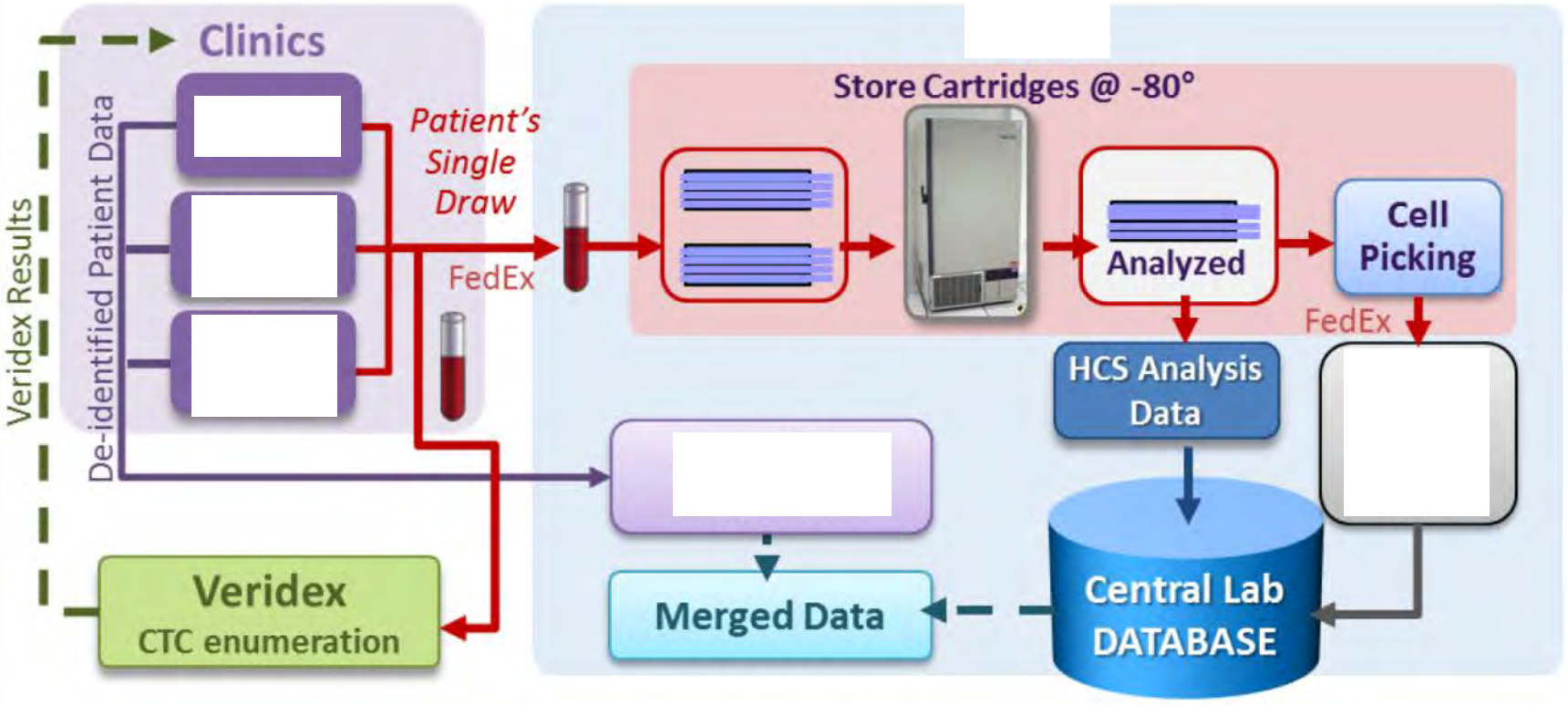
Project Objective:

- Strengthen the research use and clinical utility of HCS CTC assays
- Develop SOPs using the best pre-analytical conditions for blood CHP (collection, handling, processing)
  - Blood collection tube type (Streck, EDTA, Citrate, Heparin)
  - Time to assay (24 and 72 hours)

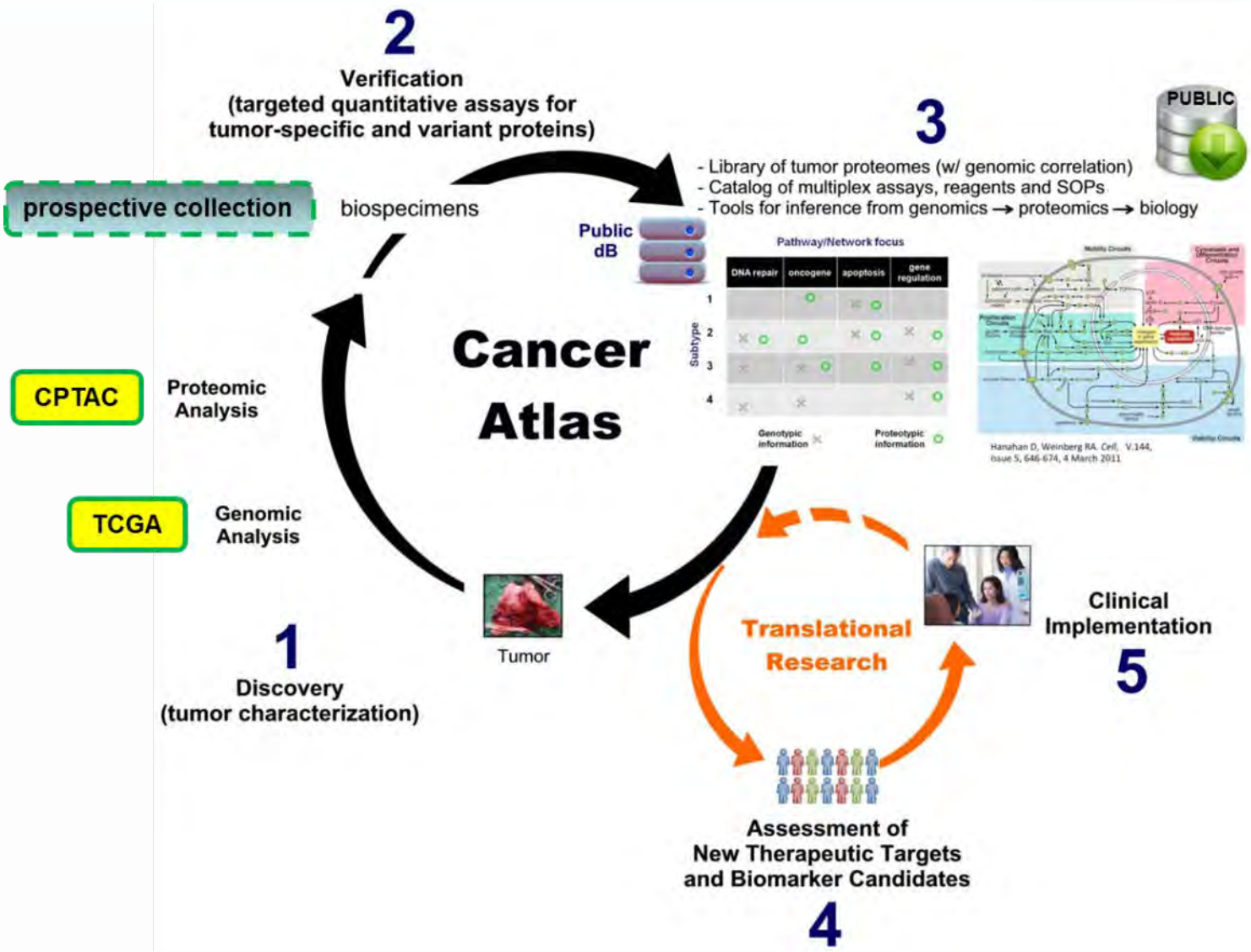


Key Pilot Output: Public Release of Data

Results will be compared to the Veridex CellSearch® system and **will be deposited in a publically available database**



Is There A Place for CTCs…



Personal Prediction…

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"LOTS of Quantitative and Reproducible Data"

Saturated steam					Superheated steam	
Pressure (kg/cm²)	Temp (°C)	Vapour enthalpy (kcal/kg)	Specific volume (m³/kg)	Density (kg/m³)	Specific volume (m³/kg) at 250°C	at 300°C
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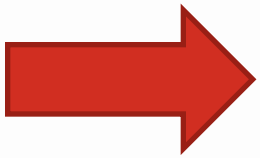
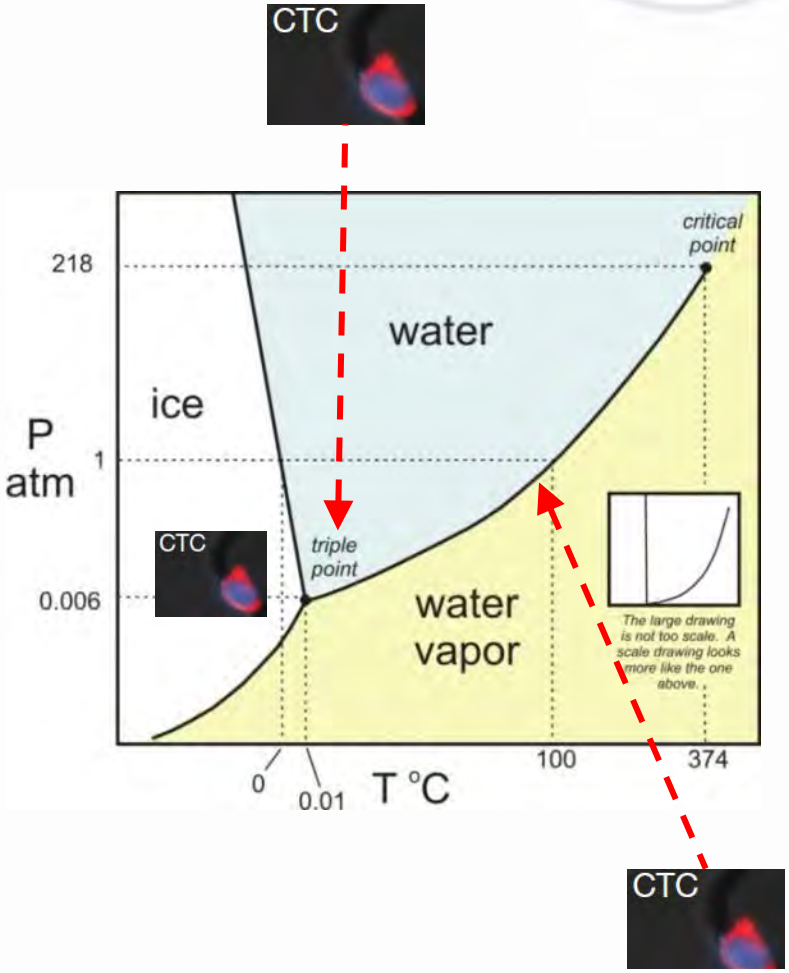




Relevant CSSI Funding Opportunities

Center for STRATEGIC Scientific Initiatives

http://cssi.cancer.gov/resources-current_funding.asp

Provocative Questions ($30M)

Due Date 12/04/12

- **Research Answers to NCIs Provocative Questions**
  - **Group A:** RFA-CA-12-015 (R01) **[$5-$7M]**
    RFA-CA-12-016 (R21) **[$2-$3M]**
  - **Group B:** RFA-CA-12-017 (R01) **[$5-$7M]**
    RFA-CA-12-018 (R21) **[$2-$3M]**
  - **Group C:** RFA-CA-12-019 (R01) **[$5-$7M]**
    RFA-CA-12-020 (R21) **[$2-$3M]**
  - **Group D:** RFA-CA-12-021 (R01) **[$5-$7M]**
    RFA-CA-12-022 (R21) **[$2-$3M]**

Innovative Molecular Analysis Technologies ($10.5M)

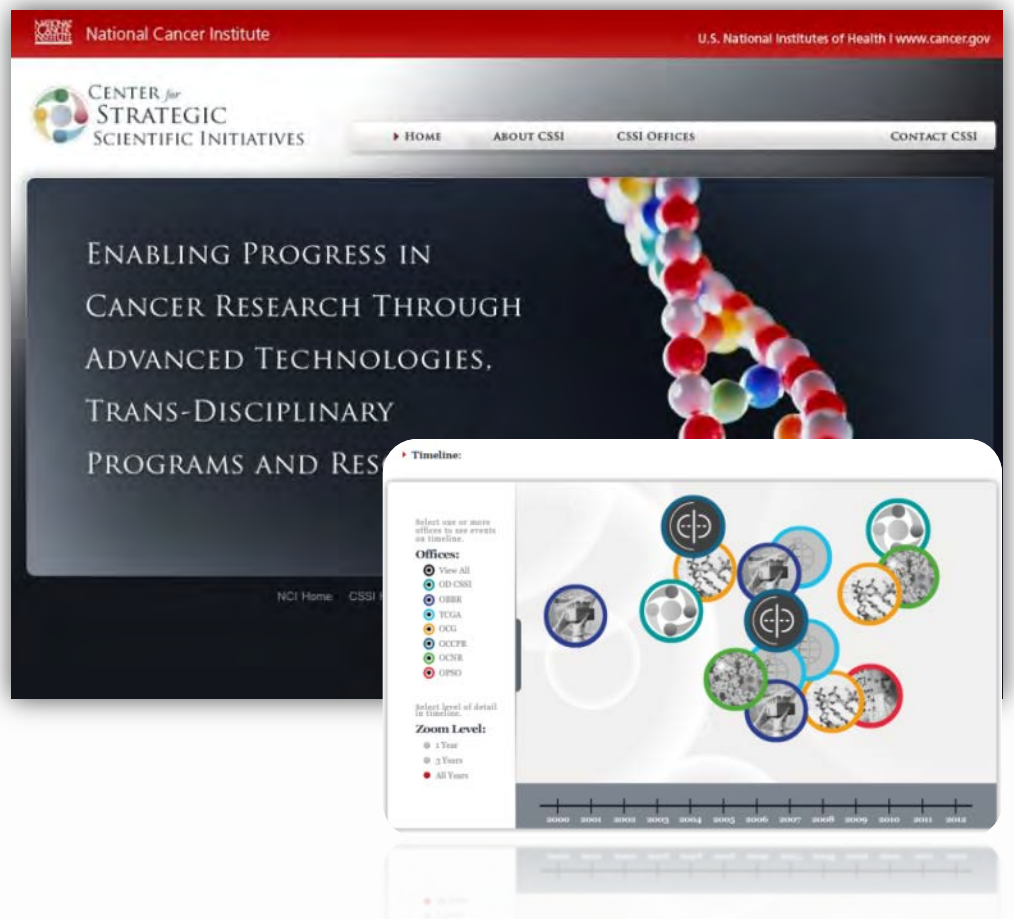
Due Date 02/20/13

- **Early-Stage Innovative Technology Development (R21)**
  - RFA-CA-13-001 (R21, 3 years) **[$5M]**
- **Validation and Advanced Development of Emerging Technologies (R33)**
  - RFA-CA-13-002 (R33) **[$3.5M]**
- **Early-Stage and/or Validating Technologies in Biospecimen Science (R21/R33)**
  - RFA-CA-13-003 (R21) **[$0.8M]**
  - RFA-CA-13-004 (R33) **[$0.7M]**

Learn More About CSSI/CCG…

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

http://cssi.cancer.gov



PQ Program Manager

Emily J. Greenspan, PhD

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